

AMENDMENTS

Please amend the claims as follows:

1.-2. (Cancelled)

3. (Previously Presented) The method of claim 20, wherein said DNA is non-genomic DNA.

4. (Previously Presented) The method of claim 20, wherein said DNA is cDNA.

5.-19. (Cancelled)

20. (Currently Amended) A method of subjecting a DNA molecule to a DNA synthesis reaction, comprising the steps of:

- a) obtaining a DNA molecule having a first linker sequence positioned at one end of the DNA molecule and a second linker sequence, different from said first linker sequence, positioned at the other end of the DNA molecule; and
- b) subjecting said DNA to a DNA synthesis reaction with a primer set comprising:
 - i) a first primer, wherein the 5' sequence of said primer is complementary to said first linker sequence and the 3' sequence of said primer comprises a specificity region; and
 - ii) a second primer, wherein the 5' sequence of said primer is complementary to said second linker sequence and the 3' sequence of said primer comprises a specificity region

wherein both the specificity regions of both the first and second primers comprise random sequences.

21. (Previously Presented) The method of claim 85, wherein said amplification is performed with an array of combinations of alternate amplification primers.

22. (Cancelled)
23. (Previously Presented) The method of claim 85, further comprising, identifying the amplified DNA.
24. (Original) The method of claim 23, wherein said identification is based upon length.
25. (Original) The method of claim 23, wherein said identification is performed by a computer program.
26. (Original) The method of claim 21, wherein said array of amplifications is performed in a multi-well plate.
27. (Original) The method of claim 20, wherein the specificity region of the primers of the first primer set is 3,4,5,6,7 or 8 base pairs long.
28. (Original) The method of claim 20, wherein the specificity region of the primers of the second primer set is 3,4,5,6,7 or 8 base pairs long.
29. (Previously Presented) The method of claim 85, wherein said amplification comprises polymerase chain reaction, nucleic acid sequence based amplification, transcription mediated amplification, strand displacement amplification or ligase chain reaction.
30. – 35. (Cancelled)
36. (Previously Presented) The method of claim 85, wherein a label is incorporated into said amplified DNA.
37. (Original) The method of claim 36, wherein said label is incorporated by means of a labeled primer.

38. (Original) The method of claim 36, further comprising, partial nucleotide sequence identification of the amplified products by the identity of the label.
39. (Original) The method of claim 36, wherein said label is a chromophore.
40. (Original) The method of claim 36, wherein said label is a fluorophore.
41. (Original) The method of claim 36, wherein said label is an affinity label.
42. (Original) The method of claim 36, wherein said label is a dye.
43. (Original) The method of claim 37, wherein the 5' end of said primer comprises an amino moiety and a fluorophore is covalently attached by the reaction of a succinimido ester of the fluorophore to the 5' amino-modified primer.
44. (Original) The method of claim 40, wherein said fluorophore is Alexa 350, Alexa 430, AMCA, BODIPY 630/650, BODIPY 650/665, BODIPY-FL, BODIPY-R6G, BODIPY-TMR, BODIPY-TRX, Cascade Blue, Cy2, Cy3, Cy5,6-FAM, Fluorescein, HEX, 6-JOE, Oregon Green 488, Oregon Green 500, Oregon Green 514, Pacific Blue, REG, Rhodamine Green, Rhodamine Red, ROX, TAMRA, TET, Tetramethylrhodamine, and Texas Red.
45. (Previously Presented) The method of claim 20, wherein the products of said DNA synthesis reaction are analyzed.
46. (Previously Presented) The method of claim 45, wherein said analysis of products is by polyacrylamide gel electrophoresis.
47. (Previously Presented) The method of claim 45, wherein said analysis of products is by capillary gel electrophoresis.

48. (Previously Presented) The method of claim 45, wherein said analysis of products is by mass spectrophotometry.
49. (Previously Presented) The method of claim 45, wherein said analysis of products is by energy transfer.
50. (Previously Presented) The method of claim 45, wherein said analysis of products is by a filtration and extraction device.
51. (Previously Presented) The method of claim 45, wherein said analysis of products is by the use of interlaced lasers and multiple fluorescent measurements.
52. (Previously Presented) The method of claim 45, wherein said analysis of products comprises quantifying amplification products.
53. (Previously Presented) The method of claim 52, wherein said quantifying is by measuring the ratio of each product to a co-amplified reference-gene.
54. (Previously Presented) The method of claim 52, wherein said quantifying is by measuring the ratio of each product to a panel of reference-genes.
55. (Previously Presented) The method of claim 52, wherein said analysis of products is by Real-Time PCR.
56. (Previously Presented) The method of claim 45, wherein said analysis of products is performed in a multi-well plate.
57. (Previously Presented) The method of claim 45, wherein said analysis of products is performed on a membrane.

58. (Previously Presented) The method of claim 45, wherein said analysis of products is performed on a solid matrice.
59. (Original) The method of claim 58, wherein said solid matrice is a DNA chip.
60. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on DNA derived from a different cell or tissue.
61. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on DNA derived from a cancerous cell or tissue.
62. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on DNA derived from a cell or tissue treated with a pharmaceutical compound.
63. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on DNA derived from a cell or tissue treated with a teratogenic compound.
64. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on DNA derived from a cell or tissue treated with a carcinogenic compound.
65. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on DNA derived from a cell or tissue treated with a toxic compound.
66. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on DNA derived from a cell or tissue treated with a biological response modifier.

67. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on DNA derived from a cell or tissue treated with a hormone, a hormone agonist or a hormone antagonist.

68. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on DNA derived from a cell or tissue treated with a cytokine.

69. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on DNA derived from a cell or tissue treated with a growth factor.

70. (Previously Presented) The method of claim 20, performed on DNA derived from a normal cell or tissue and on the DNA derived from a cell or tissue treated with the ligand of a known biological receptor.

71. (Previously Presented) The method of claim 20, performed on more than one sample of DNA, wherein the DNA samples are derived from a cell or tissue type obtained from different species.

72. (Previously Presented) The method of claim 20, performed on more than one sample of DNA, wherein the DNA samples are derived from a cell or tissue type obtained from different organisms.

73. (Previously Presented) The method of claim 20, performed on more than one sample of DNA, wherein the DNA samples are derived from a cell or tissue at different stages of development.

74. (Previously Presented) The method of claim 20, performed on more than one sample of DNA, wherein the DNA samples are derived from a normal cell or tissue and derived from a cell or tissue that is diseased.

75. (Previously Presented) The method of claim 20, performed on more than one sample of DNA, wherein the DNA samples are derived from a cell or tissue cultured in vitro under different conditions.

76. (Previously Presented) The method of claim 20, performed on the DNA derived from a cell or tissue from two organisms of the same species with a known genetic difference.

77.-84. (Cancelled)

85. (Previously Presented) The method of claim 20, wherein the first and second primers are employed to amplify the DNA molecule.

86. (Previously Presented) The method of claim 20, wherein the first and second primers are employed to sequence the DNA molecule

87. (Currently amended) A pair of primer molecules ~~having~~ wherein both members of the pair comprise (a) a predetermined 5' sequence that ~~is prepared to incorporate~~ a sequence that anneals to a predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the specificity region defined as one of all possible sequence combinations of A, T, G and C.

88. (Currently amended) A population of paired primer molecules, the primer molecule pairs having (a) a predetermined 5' sequence that ~~is prepared to incorporate~~ a sequence that anneals to a predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the population of primer molecules having specificity regions collectively reflecting all possible sequence combinations of A, T, G and C.

89. (Currently Amended) A primer molecule pair selected from the population of claim 88.

REMARKS AND RESPONSE TO OFFICIAL ACTION

I. Claims in the Case

Claims 20 and 87-89 have been amended. Claims 3, 4, 20, 21, 23-29, 36-76 and 85-89 are pending.

II. Rejection of Claims Under Section 102(e) over Kuiper

The subject Action first rejects claims 20, 23-24, 27-29, 36-38, 45-46, 50, 71-72, 85 and 87-89 as anticipated by the Kuiper *et al.* patent. The Action takes the position that the disclosure contained in Figures 10-11 of Kuiper anticipate the indicated claims.

In response, Applicants respectfully point out that Kuiper requires the use of primer sets (*i.e.*, corresponding “left hand” and “right hand” primers) that have dissimilar specificity regions, with one member of the primer set having a known, predetermined specificity region sequence and the other member of the primer set having a random specificity region. This is evident from the Kuiper disclosure. Applicants refer the Examiner, for example, to the disclosure at col. 3, lines 52-65. Here it is revealed that one member of the primer sets of Kuiper has a predetermined sequence in what we refer to as the specificity region (see lines 59-60; “...and at the 3’ end at least 5 nucleotides matching the sequence of the simple sequence repeat ...”) and the other member of the primer set having random nucleotides in what we refer to as the specificity region (lines 63-65). We further refer the Examiner to col. 4, lines 34-43, and col. 5, lines 40-53.

In contrast, the present invention contemplates that *both* members of the primer sets incorporate random nucleotide sequences in their respective specificity regions. Furthermore,

we have been unable to identify any teaching or suggestion from Kuiper which might be used to suggest the use of primer sets having such attributes. If the Examiner is aware of such disclosure it is requested that such disclosure be identified.

III. Obvious Rejection of Claims over Kuiper *et al.*

The Action next rejects various of the dependent claims as obvious over Kuiper, alone or in combination with Matthews *et al.*

In response, Applicants incorporate by reference the comments contained in the foregoing section, and note that each of the rejected claims depend from the claims addressed in the foregoing section.

IV. Rejection of Claims 87-89 Under Section 102(a)/103 over Silver and Senapathy

The Action next takes the position that the subject matter of claims 87-89 are anticipated or obvious over the Silver '792 patent and/or the Silver *et al.* '792 patents. The Action takes the position that the relevant language of the subject claims, "that is prepared to incorporate a sequence that anneals to a predetermined linker sequence," is in fact an intended use and thus such language must be disregarded.

In response, Applicants first incorporate by reference the comments made with respect to these references in previous responses.

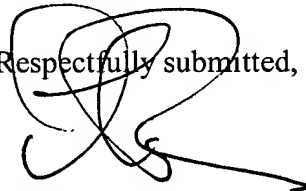
Further, Applicants note that the language referred to by the Examiner can in no way be construed as "intended use" limitations. They are, indeed, clearly structural limitations which limit the *structure* of the claimed primers. They recite no "use" whatsoever, intended or otherwise. Perhaps it is the method language "prepared to incorporate," which has led to some

confusion. Accordingly, Applicants has removed this superfluous language which should clarify the structural nature of these claim limitations.

V. Conclusion

It is submitted that the present response is a complete response to the outstanding official action, and that the claims are in condition for allowance. If the Examiner has any questions or comments, a telephone call to the undersigned at (512) 536-3055 is requested.

Respectfully submitted,

A handwritten signature in black ink, appearing to be 'D. Parker', with a long horizontal stroke extending to the right.

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